UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Addr ss: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/259,389	02/26/99	GEORGOPOULOS K	10287/043001

HM22/1001

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EXAMINER	
WOITACH, J	
ART UNIT	**PAPER NUMBER**
1632	13

DATE MAILED: 10/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application N . 09/259,389	Applicant(s) GEORGOPOULOS ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-14 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *6-9,12,14 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,10,11,13 and 18-21* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment filed July 9, 2001, Paper No. 12, has been received and entered. Claims 4, 15 and 16 have been canceled. Claims 1-3, 5, 10 and 11 have been amended. Claims 18-21 have been added. Claims 1-3, 5-14, and 16-21 are pending. Claim 6-9, 12, 14 and 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-3, 5, 10, 11, 13 and 18-21 are currently under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the specification does not contain literal or figurative support for the recitation and embodiment of

'differs at 1 or more, but not more than 15 residues'. After a review of the specification, Examiner could not find this specific embodiment, and after a review of sequence homologies among the three SEQ ID NOs could not find figurative support for such a limitation.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claim 20 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to

determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure*" (emphasis added).

Claims 15 and 16 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

Claims 15 and 16 have been canceled, obviating the basis of the rejection.

Claims 1, 3, 5, 10, 11, 13 stand rejected and claim 20 is newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants point out that the claims as amended now recite 80% identity to the sequence listings and that the encoded polypeptide have a Hellos biological activity. Applicants argue that the instant specification provides three species which meet the limitation of this claim; murine Hellos SEQ IN NO: 1, murine splice variant Hellos SEQ ID NO: 3, and human Hellos SEQ ID NO: 5, and thus, provide a sufficient number of species to demonstrate that Applicants were in possession of the claimed invention at the time of filing. See Applicants' amendment, bottom of page 5. Applicants' arguments have been fully considered but not found persuasive.

Amended claim 1 now encompasses a nucleic acid sequence which is at least 80% identical to SEQ ID NO: 1, 3, or 5 and encodes a protein with Hellos biological activity. SEQ ID NO: 1 is a polynucleotide sequence which encodes murine Hellos polypeptide, and SEQ ID NO: 3 is a polynucleotide sequence which encodes a murine splice variants identified by RT-PCR whose open reading frame could encode a variant murine Hellos polypeptide, and SEQ ID NO: 5 is a polynucleotide sequence which encodes human Hellos polypeptide. Dependant claims 3-5 encompass a nucleic acid which hybridizes to SEQ ID NO: 1, 3, or 5, encodes protein which reacts with an antibody specific for the amino acid sequence encoded by SEQ ID NO: 1, 3, or 5 and any fragment of at least 60 amino acids in length. Newly added claim 20 encompasses a nucleic acid sequence encoding a polypeptide which differs from SEQ ID NOs: 2, 4, and 6 by 1 or more residues, but nor more than 15 residues.

First, as noted in previous office action,

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

The instant specification appears to disclose three polynucleotide sequences encoding a family of Hellos proteins, SEQ ID NO: 1, 3, and 5. The only relevant identifying characteristic disclosed in the specification is that the sequences must encode proteins having appropriate biological activity. However, no correlation has been disclosed between any sequence which is 80% identical sequence and any protein structure which is sufficient for a particular biological

activity. The specification teaches that the polypeptides set forth in SEQ ID NOs: 2, 4 and 6 have the inherent biological function of Hellos protein as a transcription factor, which functions in concert with other polypeptides which are part of the Ikaros gene family. However, the specification does to describe sequences which have this biological function for any sequence 80% identical to SEQ ID NO: 1, 3, or 5. The specification fails to teach and provide an adequate description defining the portions of the encoded proteins one can change and maintain any particular biological activity. The artisan is left to empirically guess and experiment on the possible changes one can make and maintain any activity.

Second, as noted in the written description requirement,

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

In the instant case, each isolated sequence represents a genus in itself, and can not be compared one to the other as common species. Each sequence represents a unique sequence isolated from nature, and not a variant of one 'wild type' form of Hellos. The specification does not teach that all the inherent biological activities of one Hellos protein is the same as that of a second. For example, the two murine sequences which appear to be splice variants of each other share a high amount of identity, and Examiner would agree that because they share identity within a given sequences, the identical sequences would have the same biological activity. However, the

specification is silent to the function of the splice variant sequences and what extra biological activities the protein may or may not have as a consequence. The two murine sequences represent different and unique Hellos proteins which would not anticipate one another. Further, while the human sequence share homology with the murine sequences, it is unclear which of the two murine sequences the human isolate represents, and may in fact represent a completely different family member. Like the other Ikaros proteins described in the art, the Hellos proteins share some homology, but may vary greatly in biological activity. The specification fails to describe more than a single species of each genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met. Thus, for the reasons above and of record, it is maintained that the specification provides a written description only for Hellos which is encoded by nucleic acids set forth in SEQ ID NO: 1, 3, or 5.

Claims 1, 3, 5, 10 11 and 13 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants point out that the claims as amended now recite 80% identity to the sequence listings and that the encoded polypeptide have a Hellos biological activity. Applicants argue that because the claims now recite that the encoded polypeptide have Hellos biological activity the

instant specification provides adequate guidance for the generation of useful polypeptides and polynucleotides which encode them. See Applicants' amendment, page 6. Applicants' arguments have been fully considered but not found persuasive.

Examiner agrees that the specification provides adequate guidance for making SEQ ID NO: 1, 3 and 5 and use of these to make the encoded protein, and provides adequate teaching on how to make and use other nucleic acid sequences which encode a Hellos protein as set forth in SEQ ID NO: 2, 4 and 6, however the specification fails to provide necessary guidance on use of the nucleic acid sequences which do not encode a Hellos protein. Further, no guidance is given for making or using the nucleic acid sequences which meet the hybridization limitations.

As noted in the previous office action, In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case there are a large number of nucleic acid sequences which contain 'at least about 60 amino acids' and share enough homology to hybridize to the recited SEQ ID NOs, however these sequences encode various unrelated proteins. Examiner notes that the claims now recited that the encoded protein have Hellos biological activity, however this activity is not specifically defined in the specification, nor

does the specification show that the biological activity between the various mouse and human isolates are even the same. Therefore, while the specification provides the necessary guidance to make the polynucleotides set forth in SEQ ID NO: 1, 3 or 5, it does not provide the necessary guidance for one of skill in the art to use the nucleic acid sequences which do not encode a Hellos protein. Any activity of the protein encoded by the polynucleotides set forth in SEQ ID NOs would inherently have all the activities of the normal endogenous Hellos protein, however it is not clear what all these activities are and where and to what extent one can alter the endogenous sequence and maintain the inherent activities. The specification defines Hellos within the context of the Ikaros family and it is unclear what activities the protein by itself has that one can assay. Further, the Hellos sequences represent three separate genus of sequences, two murine and one human, and it is unclear if each of these sequences have the same activity or share some similarities and diverge in others. The specification fails to teach and provide an adequate description defining the portions of the encoded proteins one can change and maintain any particular biological activity. The artisan is left to empirically guess and experiment on the possible changes one can make and maintain any activity.

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time the invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed, and therefore the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 10, 11, 13 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 1, 3 and 20 are vague and unclear in the recitation of 'a Hellos activity' because what Hellos activity is encompassed by the claim is not clearly defined. A Hellos biological activity is not specifically defined in the specification and it is unclear what the metes and bounds of such an activity would be. Any activity of the protein encoded by the polynucleotides set forth in SEQ ID NOs would inherently have all the activities of the normal endogenous Hellos protein, however it is not clear what all these activities are and where and to what extent one can alter the endogenous sequence and maintain the inherent activities. The specification defines Hellos within the context of the Ikaros family and it is unclear what activities the protein by itself has that one can assay. Further, the Hellos sequences represent three separate genus of sequences, two murine and one human, and it is unclear if each of these sequences have the same activity or share some similarities and diverge in others. It is not clear if a complete functional protein is made maintaining all biological activities or if the claim also includes fragments having one activity, such as binding DNA or diamerizing with other Ikaros family members. It is unclear if the claims encompass short fragments with limited biological activity or even chimeric proteins.

Claims 3 and 5 are vague and indefinite in the recitation of "under high stringency conditions" because the conditions are not specifically described in the specification or the claim, so the metes and bounds have not been adequately defined. Though the instant specification has been amended to recite hybridization conditions cited in *Current Protocols in Molecular Biology*, these conditions are only examples as recited in the incorporated text (applicants amendment paper number 8; page 1, third line-entered on page 56; line 30). Since these are only examples, the specific conditions for stringent hybridization are still not adequately defined. Dependent claims are included in the rejection because they fail to clarify the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5 rejected under 35 U.S.C. 102(a) as being anticipated by Hahm *et al.* is withdrawn.

Applicants declaration filed under 37 CFR 1.131 establishing a date of invention prior to February 4, 1998, before the Hahm *et al.* publication date overcomes this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10, 11 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over Hahm *et al.* in view of Molnar *et al.* is withdrawn.

Applicants declaration filed under 37 CFR 1.131 establishing a date of invention prior to February 4, 1998, before the Hahm *et al.* publication date overcomes this rejection.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 19 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 21. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 19 is dependent claim 1, however both claims 19 and 21 encompass the exact same scope. Both claims 19 and 21 are drawn to a nucleic acid sequence encoding a polypeptide set forth in SEQ ID NOs: 2, 4 and 6.

Conclusion

No claim is allowed. The claims are free of the art of record because the art fails to teach the three Hellos family members; murine SEQ ID NO: 1, murine splice variant SEQ ID NO: 3 and human SEQ ID NO: 5. However, the instant claims encompass polynucleotide sequences which share only some homology with the sequences set forth in SEQ ID NOs and are subject to other rejections. Claim 2 would be found allowable if rewritten in independent form, and either claim 19 or 21 would be found allowable if one or the other is amended.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached at (703)305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to Kay Pinkney whose telephone number is (703)306-3076.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Deborah Crouch

Joseph T. Woitach

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